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The excursion model for MAP kinase signaling in health and disease

Elizabeth J Goldsmith

University of Texas Southwestern Medical Center at Dallas, USA

MAP kinase modules, a cascade of three kinase enzymes, a MAP3K, MAP2K and MAPK, propagate diverse extracellular signals to downstream effectors. The two double phosphorylation reactions catalyzed by the modules occur in a precise order that maximizes the number of reaction steps between signal and final activation. Activation is associated with the final Thr phosphorylation of the MAPK. The observed order of phosphorylation events suggests an excursion from the Ser/Thr kinase activity of the MAP3K into Tyr kinase activity of the central dual specificity MAP2K and back to Ser/Thr kinase activity, thus the reaction order and the tempo of MAPK activation changes in cancer mutants of the MAP2K.

Biography

Elizabeth J Goldsmith has received her PhD in Physical Chemistry at UCLA, worked with Dave Eisenberg, Max Perutz and Robert Fletterick and has been at UT Southwestern Medical Center at Dallas for 27 years, in the Department of Biophysics. Her publications concern structural biology and biochemistry of protein kinases and other conformationally regulated proteins.

Elizabeth.goldsmith@utsouthwestern.edu

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